REMARKS

This Response, filed in reply to the Office Action dated March 17, 2008, is believed to be fully responsive to each point of objection and rejection raised therein. Accordingly, favorable reconsideration on the merits is respectfully requested.

Claims 1 and 4-6 remain rejected in the application. Consideration of the remarks herein is respectfully requested.

Claims 1 and 4-6 are Patentable Under 35 U.S.C. § 103

1. On page 2 of the Office Action, Claims 1 and 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0583665 ("EP '665") in view of either Aikawa (7,101,532; "Aikawa '532"), Kitaguchi (7,008,614; "Kitaguchi"), or Schmidt (6,077,529; "Schmidt"), for reasons of record. For brevity, these reasons are not reiterated herein.

In addition to the rejection of record, the Examiner also purports that Applicants' data provided in the Rule 132 Declaration filed January 17, 2008, are not unexpected. Specifically, the Examiner appears to take the position that the compound in sample 2 is not encapsulated within the liposomes, and therefore one of ordinary skill in the art would not expect any uptake by macrophages.

Applicants respectfully disagree, and respectfully traverse the rejection on the following grounds.

In making the rejection, the Examiner alleges that one of ordinary skill in the art would readily have encapsulated or incorporated the benzimidazole compounds of EP '665 in liposomes, citing Aikawa '532 and Kitaguchi in support. However, Applicants note that the secondary references do not even suggest using a liposome having phosphatidylcholine and

phosphatidylserine in a ratio of 1:1. Of the references cited by the Examiner, only WO 97/35560, cited in the Office Action mailed July 28, 2006, discloses *incorporation* of a compound into the *membrane* of a liposome, by addition of the compound after formation of the liposome. In the secondary references relied upon by the Examiner to support an assertion of obviousness, the liposomes were merely mixed with compounds, and no evidence is provided that the compounds were incorporated into the liposome membranes. Further still, the phospholipid components of the liposomes of the secondary references differ with respect to phospholipid type and ratio, and with respect to the active compound to be administered, from both EP '665 and WO 97/35560. Applicants point out that it is entirely unpredictable which compounds may be *incorporated into the membrane* of a liposome of a given phospholipid formulation, and vice versa. In other words, incorporation of a compound into liposomal membranes is influenced not only by the compound to be incorporated, but also by the specific types and ratios of phospholipids present in the liposome. For this reason, one of ordinary skill in the art would have no expectation of success that the claimed benzimidazole compounds would be *incorporated* into liposomes containing phosphatidylcholine and phosphatidylserine in a ratio of 1:1, as is required to maintain a finding of obviousness.

Such unpredictability is confirmed by Applicants' additional experiments which confirm that the benzimidazole compound was successfully incorporated into the liposome disclosed in WO 97/35560, even after formation of the liposome, whereas the benzimidazole compound was not incorporated into a liposome wherein phosphatidylcholine and phosphatidylserine are at a ratio of 1:1, when the benzimidazole compound was added after the formation of the liposome. One of ordinary skill in the art would understand from the state of the art that it is entirely unpredictable whether a given liposome formulation would incorporate a particular compound as

a membrane component, and that the type of compound, and the types and ratios of phospholipids present in the liposome, all influence whether incorporation occurs or not. Applicants respectfully submit that the Examiner has failed to consider such unpredictability in asserting obviousness, because none of the cited references provide any expectation of success that the claimed benzimidazole compounds could be incorporated as a membrane component into liposomes wherein phosphatidylcholine and phosphatidylserine are at a ratio of 1:1.

Although the Examiner relies upon the holding in *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, 82 USPQ2d 1385 (2007) to support the rejection, Applicants note that even in light of *KSR*, a finding of obviousness requires that the expected results be predictable to one of ordinary skill in the art. As discussed above, it is entirely unpredictable what liposome formulations will incorporate what compounds as membrane components, therefore *KSR* does not apply.

For the foregoing reasons, Applicants respectfully submit that the instant claims are not rendered obvious by the cited references.

Withdrawal of the rejection is respectfully requested.

2. On page 3 of the Office Action, Claims 1 and 4-6 are rejected under 35 U.S.C. §103(a) as being unpatentable over Aikawa (5,387,600; "Aikawa '600") in view of either Aikawa '532, Kitaguchi or Schmidt, for reasons of record. For brevity, these reasons are not reiterated herein.

In addition to the rejection of record, the Examiner again purports that Applicants' data provided in the Rule 132 Declaration filed January 17, 2008, are not unexpected. Specifically, the Examiner appears to take the position that the compound in sample 2 is not encapsulated

within the liposomes, and therefore one of ordinary skill in the art would not expect any uptake by macrophages.

Applicants respectfully disagree, and respectfully traverse the rejection on the following grounds.

As discussed above, one of ordinary skill in the art would understand that it is entirely unpredictable whether a given liposome formulation would *incorporate* a particular compound as a membrane component, and that the type of compound, and the types and ratios of phospholipids present in the liposome, all influence whether incorporation occurs or not. Therefore, Applicants submit that the cited references do not render obvious the instant claims at least for the reasons set forth above.

Further, Applicants note that none of the references cited to support the rejection even disclose a liposome containing phosphatidylcholine and phosphatidylserine at a ratio of 1:1, much less that the claimed benzimidazole compounds would be incorporated as a membrane component by such a liposome. Accordingly, not only would one of ordinary skill in the art not possess any expectation of success in arriving at the claimed invention for the reasons set forth above, but the cited references also fail to teach each and every element of the claims, as is also required to maintain a finding of obviousness.

For the foregoing reasons, Applicants respectfully submit that the instant claims are not rendered obvious by the cited references.

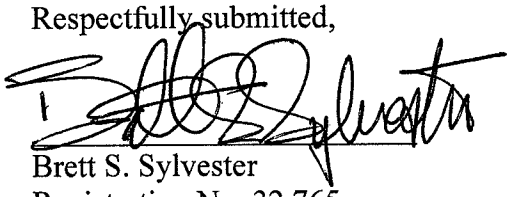
Withdrawal of the rejection is respectfully requested.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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Date: September 17, 2008